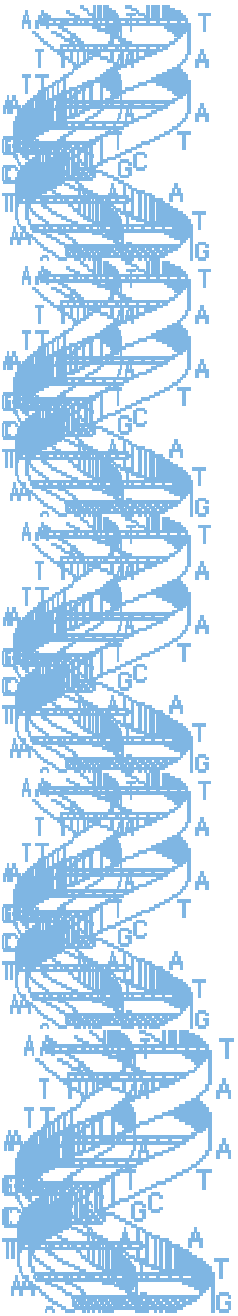


Metabolic Engineering

Metabolic Engineering of Knives Forks and Spoons

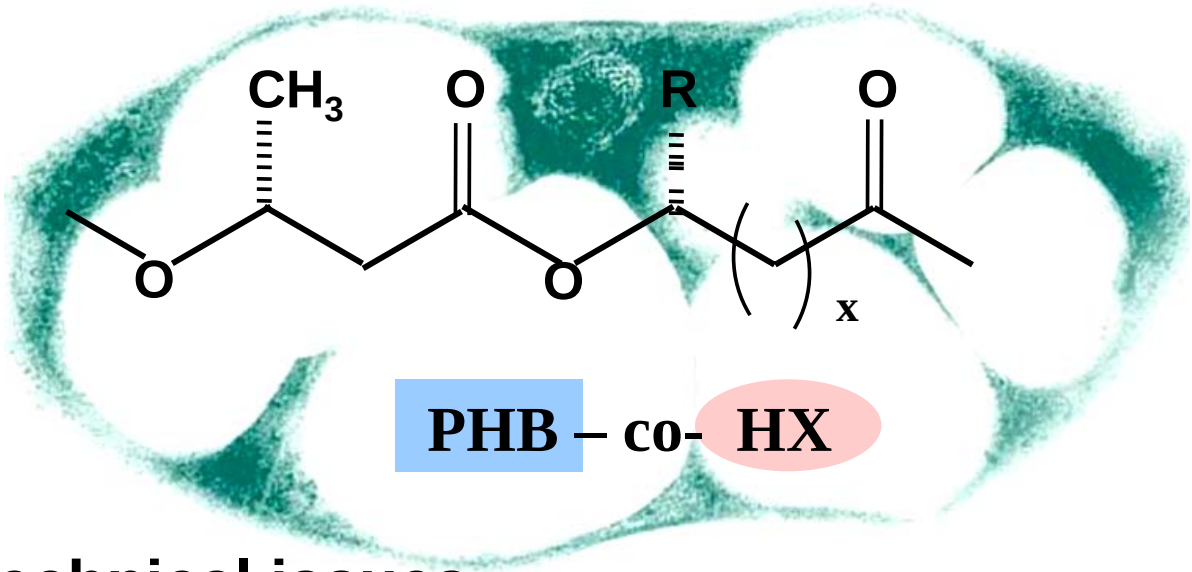
Oliver P. Peoples

Metabolix Inc.

Metabolix "The PHA Technology Company"

- **Integrated systems based approach covering the value chain**
  - **Molecular biotechnology**
    - **Metabolic engineering (hence "Metabolix")**
    - **Production strain development**
    - **PHA producing plants**
  - **Bioprocess engineering**
  - **Polymer science and engineering**

PHB Co-Polymers: A Versatile Family

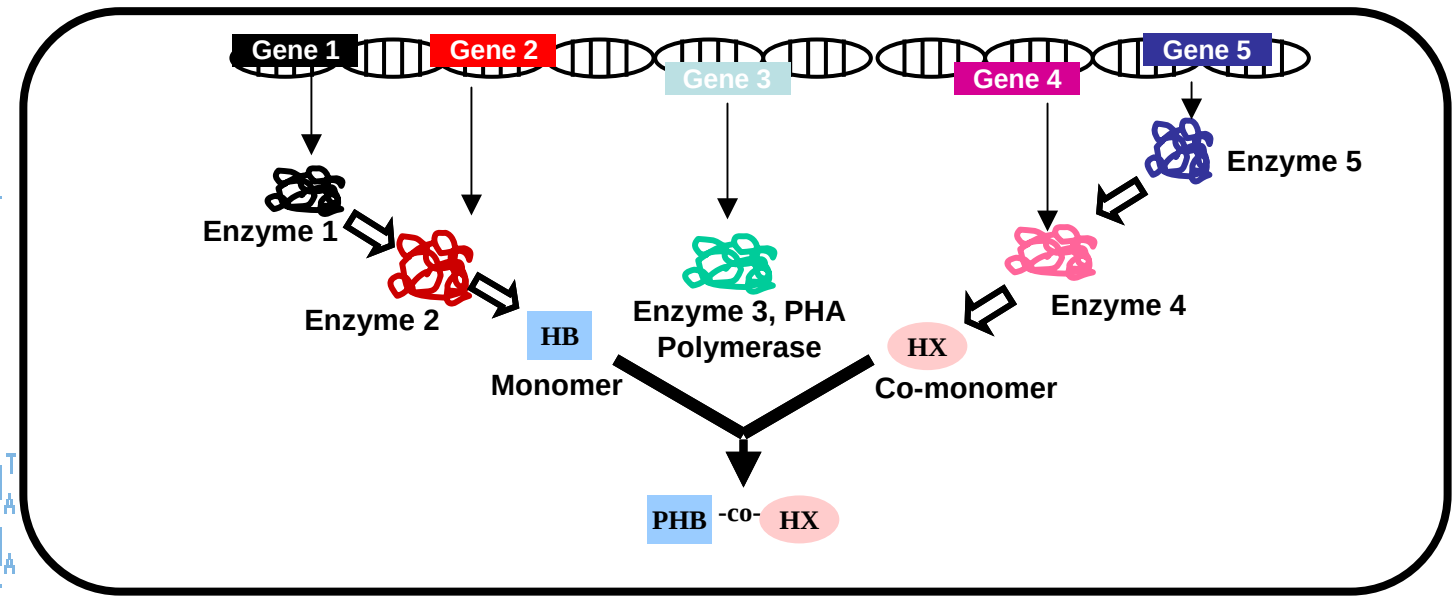


R= H to C_{11}
X= 0 to 4

- **Key technical issues**
  - **Reliable production of a copolymer inside a living cell**
    - **Control of polymer composition**
    - **Control of molecular weight**
    - **Control of polymer production vs. cell biomass**
    - **Design for manufacturing**
    - **Cost-effective process**

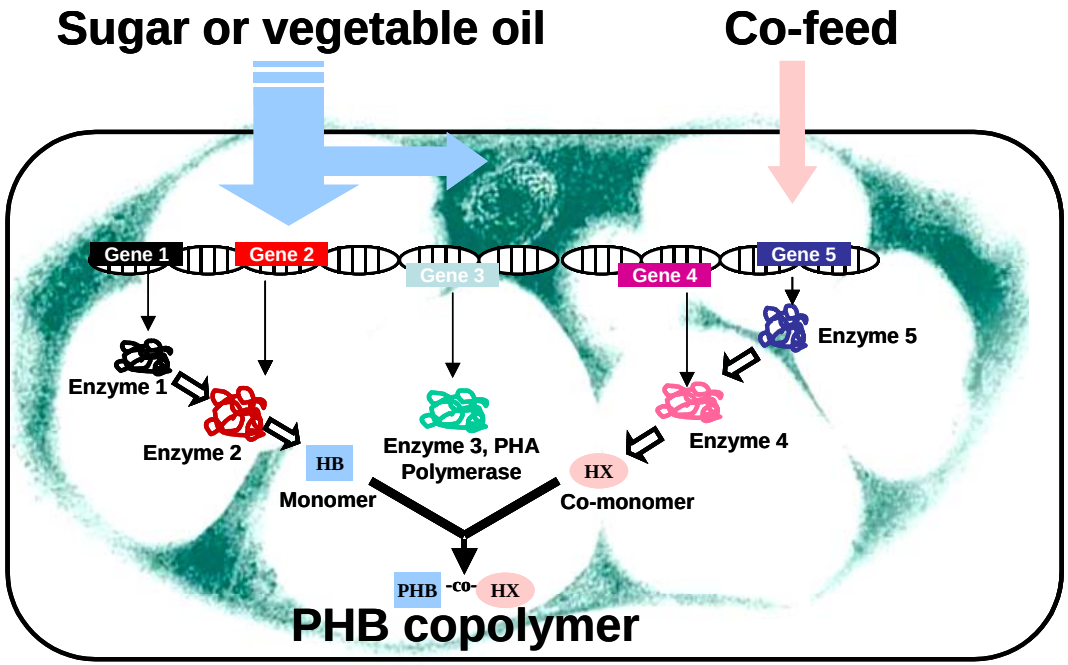
"The Designer Industrial Genome"

- **Genomics and proteomics**
  - **enable access to nature's diverse biocatalytic capabilities encoded by specific genes >** Gene 1 Gene 2 Gene 3 Gene 4 Gene 5
- **Precision genome engineering**



Production host: bacteria or plant

Cost Effective - Today!

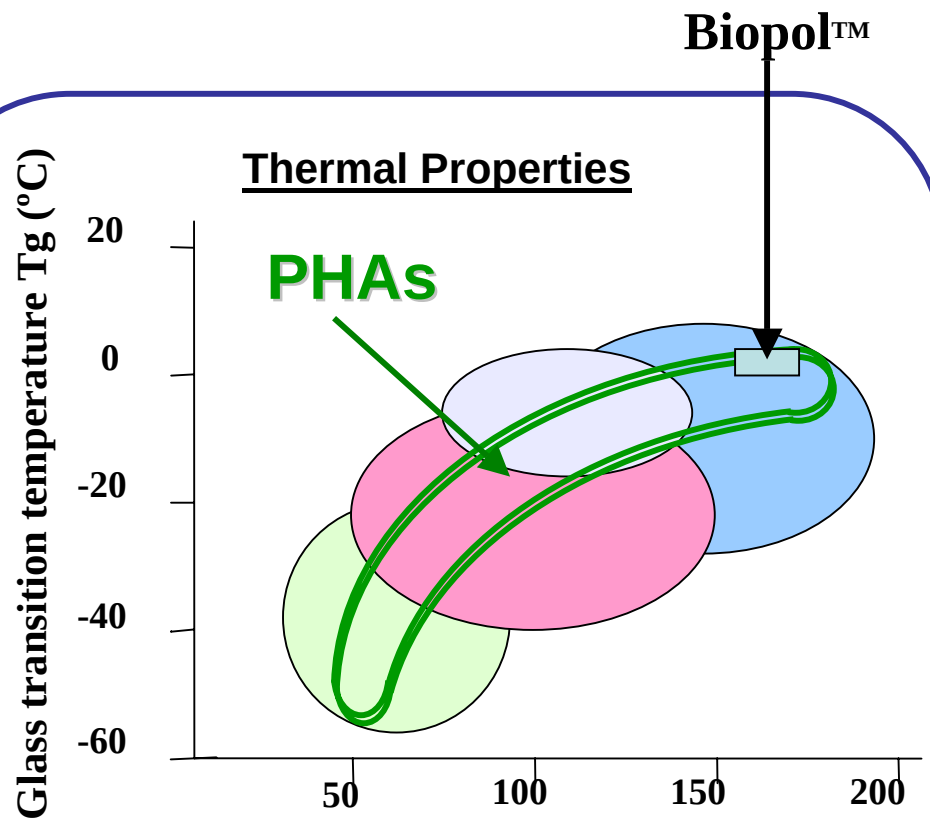


Polymer science and engineering

Process Engineering

- Common fermentation process using standard equipment
  - Highly flexible
  - Highly reproducible
  - Scaled up to 60,000L
- Common recovery process, used for all polymer compositions
  - Process validated on industrial equipment at the tonnage scale
- Manufacturing cost
  - Cost reduced sufficiently to allow significant market penetration
  - Vegetable oil at 15-20 c/lb gives cost equivalence to dextrose at 8 – 10 c/lb

PHAs Are Alternatives to >50% of Polymer Used Now



- Thermoplastics
- Hot melt adhesives
- Coatings
- Pressure sensitive adhesives

- "Very good plastics"
- Form excellent films
- Good barrier properties
- Durable in use
- Excellent UV stability
- Biodegradable

Commercialization is Underway

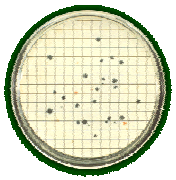
- **Strategic alliance with ADM announced (11/3/04)**
  - **Implementation of Metabolix's proprietary manufacturing technology**
  - **Construct first commercial plant (50,000 tons)**
  - **Supports broad commercial roll-out, 50/50 JV**

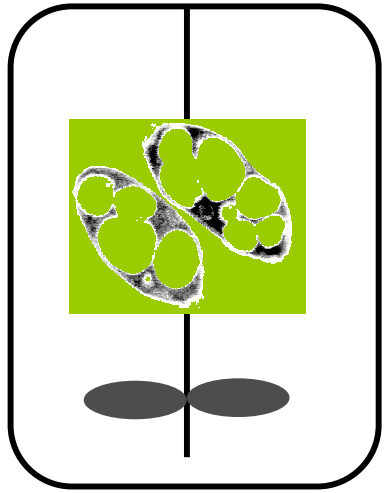
Metabolix **where nature performs™**

Metabolic Engineering (ME)

- **Biological catalyst development based on living organisms**
- **Metabolic engineering can be used to address the entire production process**
  - **Fermentation scale-up**
  - **Recovery processes**
  - **Manufacturing operations**
  - **Discovery**
  - **Selection of the production host**
  - **Lifecycle**

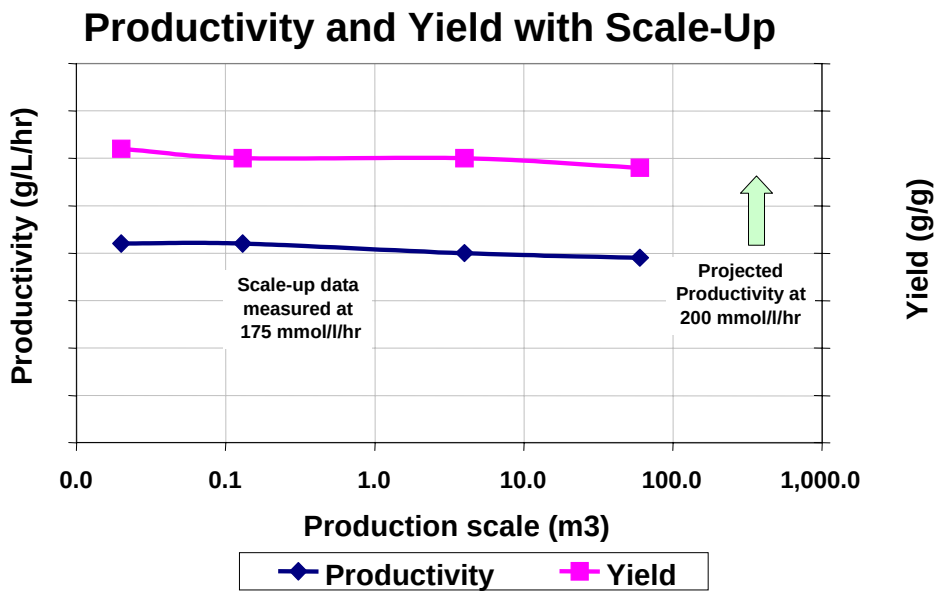
ME Impacts Scale-Up





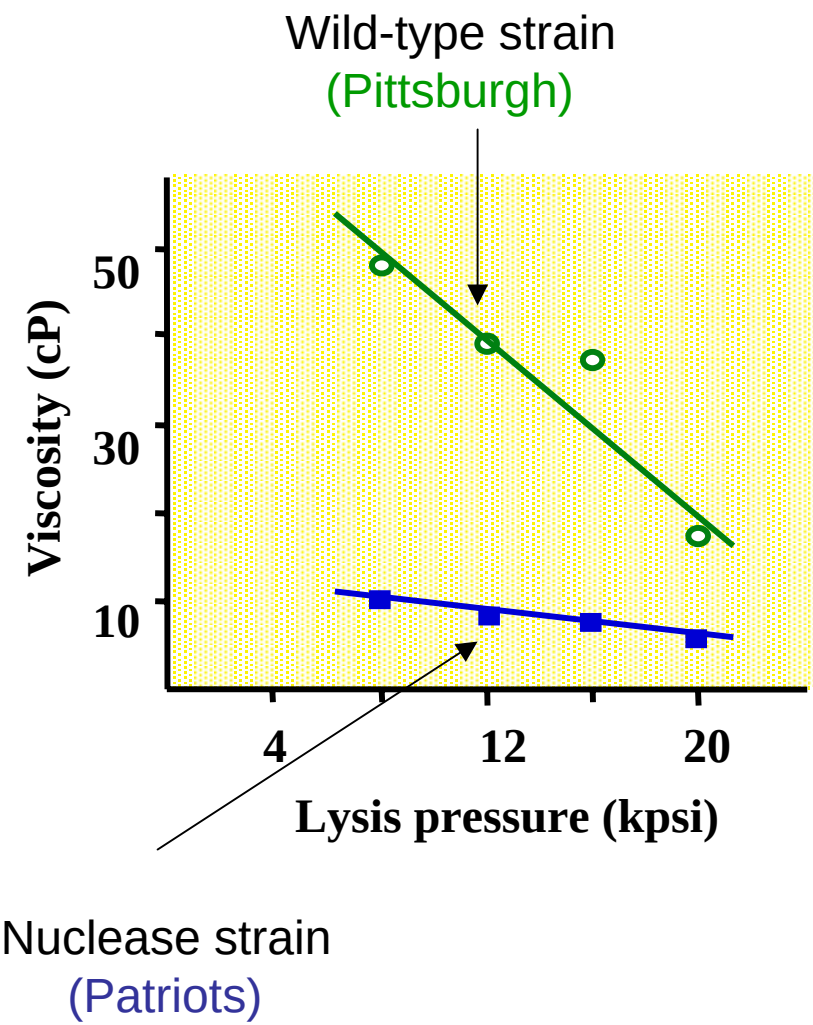
~ 35 - 40 generations, ~ 10^{17} cell divisions

10^{18} cells (300,000L)

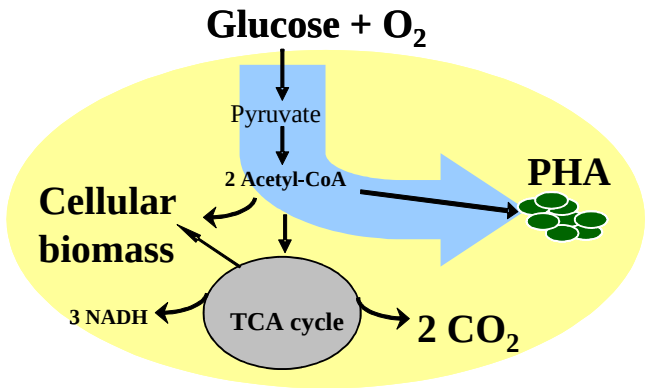


ME Impacts Recovery Process

- **Issue: to recover intracellular product results in high viscosity of lysed cells**
- **Approach: engineer production strains to express nuclease**
- **Nuclease activates on cell lysis**
- **Technology validates under production conditions**

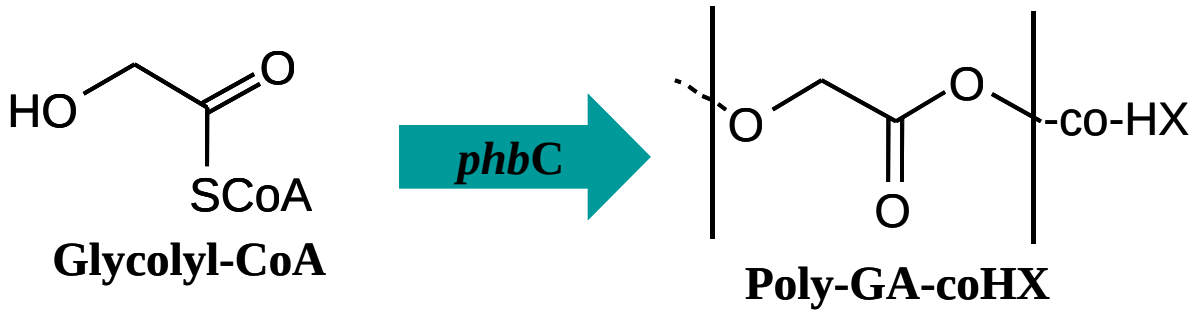


ME Impacts Manufacturing Operations



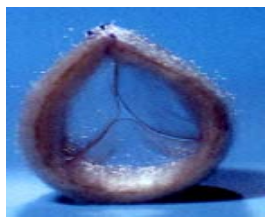
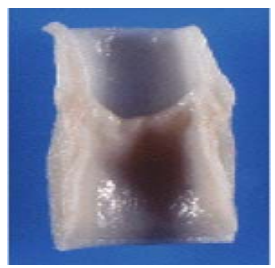
- **Objective: Improve product yield on carbon**
- **Re-engineer *E. coli* central metabolism**
- **Achieved 70% of targeted yield improvement**
- **50% yield improvement on oxygen**
  - **Reduces aeration requirements**
  - **Reduces heat load**
  - **Simplifies operations**

Discovery : Expanding the PHA Monomer Family



Glycolyl-CoA **Poly-GA-coHX**

tepha

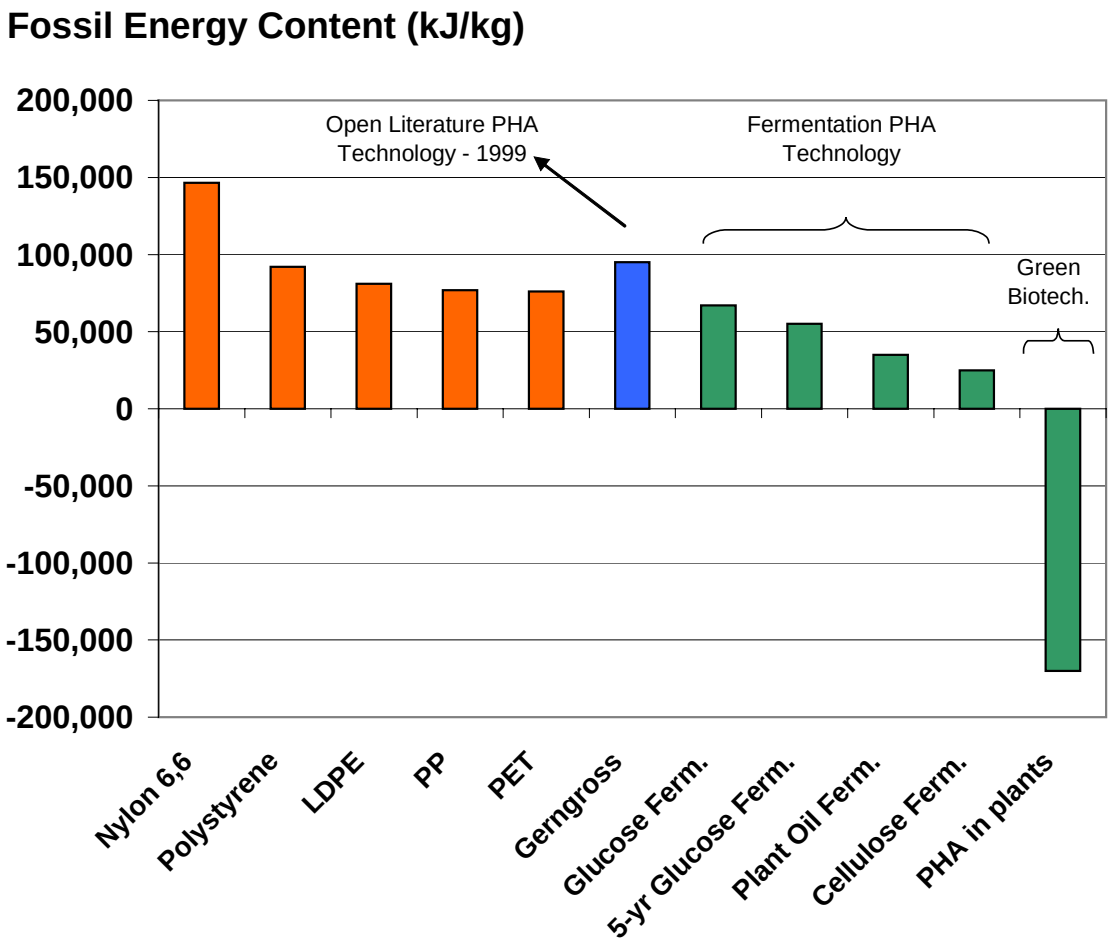




Tissue engineered heart valves

ME - Selection of Production Hosts

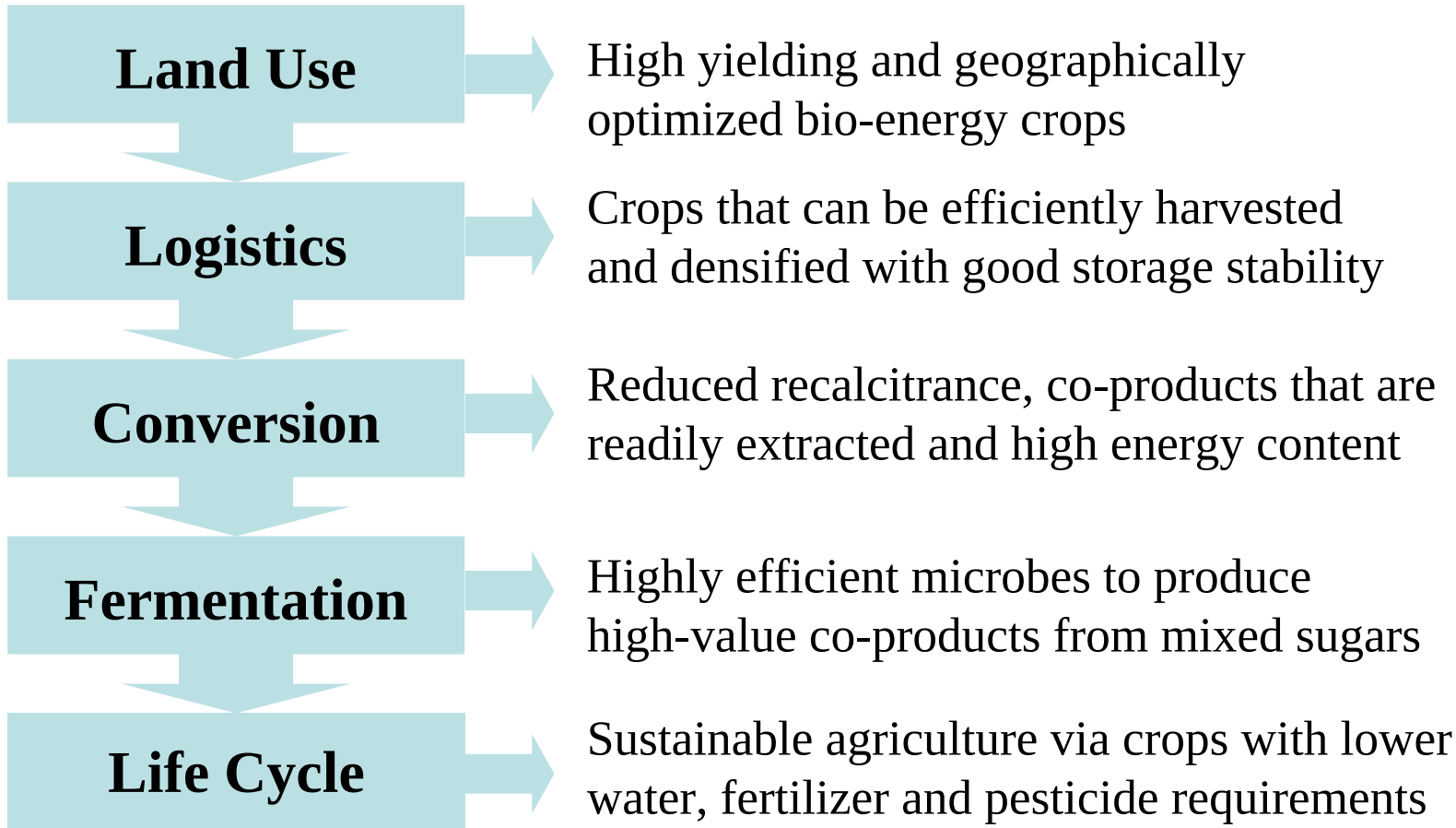
- **Goal: Coproduction of PHAs and biomass for fuels and energy**
  - **PHAs are the value-add that makes the overall system economic**
- **Status:**
  - **~10% PHA levels achieved in model plants (*Arabidopsis* and tobacco)**
  - **Inducible promoter technology demonstrated for PHA production**

ME Impacts Lifecycle of Bioproducts



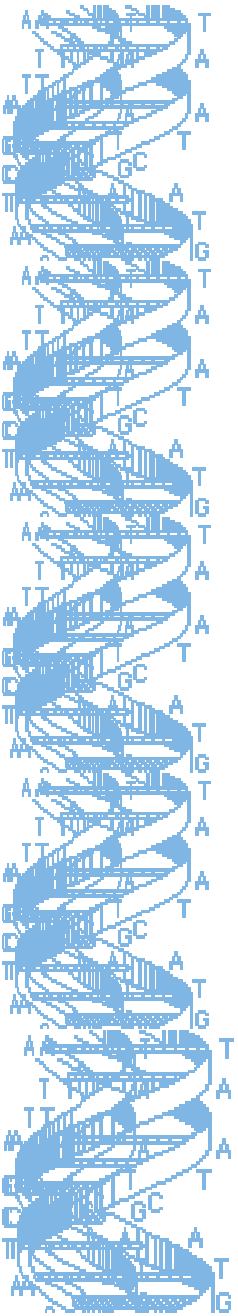
MEWG, Metabolix Inc. February 3, 2005

ME: Impacts Across the Biorefinery Value-Chain



Metabolix Inc.

- Very large market fundamental to the global economy
- Technology aligned with emerging environmental trends
- Innovative and proprietary technology to produce plastics biologically from renewable resources (PHAs)
  - Fermentation production is cost effective today
  - PHA Bioplastics are very good materials
  - PHA Bioplastics can be processed on existing equipment
- Broad and deep intellectual property position
- Metabolix will be the “PHA Technology Company”
  - Partnerships at several levels of the value chain



Metabolic Engineering

Thank You for Your Support!

Oliver P. Peoples

Metabolix Inc.